UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte EVANGELYN C. ALOCILJA and ZARINI MUHAMMAD-TAHIR

Appeal No. 2006-2198
Application No. 10/074,499

ON BRIEF

Before ADAMS, GRIMES, and GREEN, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to an immunoassay device, which the examiner has rejected as obvious. We have jurisdiction under 35 U.S.C. § 134. We affirm.

Background

The specification states that "[a]ssays based upon conductivity or resistance are well known. . . . Illustrative published art is Kim et al., Biosensor & Bioelectr[on]ics 14 907, 915 (published in February of 2000). . . . In Kim et al[.], a conductive polymer is bonded to conductive gold particles, which also serve as a visually detectable reagent, for a conductimetric assay. None of the prior art uses a capture reagent labeled with a conductive polymer in a sandwich type assay in the absence of conductive metal particles." Pages 1-2.

The specification discloses a "biosensor device which uses a fluid mobile electrically conductive polymer bound to . . . a capture reagent (such as an antibody) which captures an analyte in a fluid sample and then migrates to a capture zone where the complexed analyte is captured by another capture reagent (such as a monoclonal or polyclonal antibody) bound to . . . a substrate. The conductance or resistance is then measured." Page 1.

Discussion

1. Claim construction

Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24, and 26 are pending and on appeal. The claims subject to each rejection will stand or fall together, because Appellants have not argued them separately. See 37 CFR § 41.37(c)(1)(vii). We will focus on claims 1 and 22, which are representative of the claims subject to each rejection. Claims 1 and 22 read as follows:

> 1. A biosensor device which comprises:
>
> a strip of a substrate having at least two zones wherein a
>
> (1) first of the zones contains a first capture reagent bound to the substrate in a defined area between electrodes on different sides of the defined area for providing an electrical bias to the defined area; and
>
> (2) a second of the zones containing a fluid transfer medium for supplying a fluid to the first zone, wherein the second zone comprises a second defined area containing a second capture reagent bound to an electrically conductive polymer in absence of electrically conductive metal particles, wherein when a fluid sample containing an analyte is bound by the second capture reagent to form a complex, the complex migrates to the first zone in the medium and the analyte is bound by the first capture reagent thereby altering a conductivity or resistance of the defined area in the first zone as measured between the electrodes to detect the analyte.

22. The device of Claim 1 or 2 as a multiple array of devices grouped together separately on the substrate so that multiple analytes can be detected simultaneously from the same sample.

Claim 1 is directed to a device comprising two zones, each of which contains a capture reagent (e.g., an antibody). The two capture reagents bind to the same analyte. In the first zone, the capture reagent is immobilized between electrodes. In the second zone, the capture reagent is bound to "an electrically conductive polymer in [the] absence of electrically conductive metal particles."

The specification defines "conductive polymer" to mean "any polymer which is conductive and fluid mobile when bound to an analyte, particularly when bound with a capture reagent. . . . The polyanilines are preferred." Page 9, lines 12-28.

Claim 1 ends in a "wherein" clause that recites how the device functions: analyte in a fluid sample is bound by the second capture reagent, then the analyte/capture reagent complex is carried to the first zone by a transfer fluid, where the complex is bound by the first capture reagent and the change in the conductivity or resistance (caused by the electrically conductive polymer) is measured by the electrodes.

Claim 22 is directed to the same device "as a multiple array of devices grouped together separately on the substrate."

2. Obviousness based on Kim and Sigal

The examiner rejected claims 1, 2, 7-9, 14-16, 18, 19, and 21 under 35 U.S.C. § 103 as obvious in view of Kim[1] and Sigal.[2] The examiner characterized Kim as teaching all the limitations of instant claim 1, except for one: "Kim et al[.] fail to teach

[1] Kim et al., "Conductimetric membrane strip immunosensor with polyaniline-bound gold colloids as signal generator," Biosensors & Bioelectronics, Vol. 14, pp. 907-915 (2000)
[2] Sigal et al., U.S. Patent 6,319,670, issued Nov. 20, 2001

that the complex is formed in the absence of any electrically conductive metal particles in the complex." Examiner's Answer, page 5.

The examiner cited Sigal as "teach[ing] that it is generally known in the art to create microparticles using conductive material from a variety of alternative sources, including metals such as gold and organic polymers such as polyaniline. . . . See column 4, line 52 to column 5, line 32. The examiner concluded that "it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute an organic polyaniline polymer for gold metal, since Sigal et al[.] teach that the materials to make electrically conductive microparticles are interchangeable and suitable for the same purpose." Id., page 6.

We agree with the examiner that the cited references would have made the instantly claimed device prima facie obvious. The device disclosed by Kim is identical to the device of claim 1, except that the second (mobile) capture reagent is bound to both a gold particle and an electrically conductive polymer and therefore is not bound "in [the] absence of electrically conductive metal particles." Kim discloses that gold particles were used as a label in order to test the approach of quantitating the immunoassay signal based on a change in electrical conduction. See page 908, left-hand column:

> There is an intriguing approach whereby because the colloid particles contain metal, the gold density formed on the membrane surface may vary the electric conduction along the metal particles. . . .
>
> . . . [W]e have explored thick-film electrodes screen-printed on nitrocellulose membranes that were also used as solid matrix for antibody immobilization, and a suitable signal generator for conductimetric measurement by utilizing colloidal gold . . . modified with a conducting polymer.

Kim explains that gold particles performed poorly when used alone as a label, perhaps because of proteins forming a shell around the gold particles and inhibiting "electron hopping." Page 913, paragraph bridging the columns. Kim teaches that polyaniline polymers were attached to the surface of the gold particles to "bridge the neighboring particles or at least bring them closer to improve the charge-transfer state." Page 913, right-hand column. Kim discloses that addition of polyaniline to the gold particles "enhanced the electric conduction." Id.

Sigal teaches the use of electrically conductive microparticles in electrochemi-luminescence assays. See the abstract. Sigal teaches that "[t]he preparation of conductive particles is well known in the art. . . . For example, conductive microparticles may be prepared that comprise metals, for example, gold, silver, platinum, palladium, zinc, iron, nickel, lead, and copper. . . . Conductive microparticles may comprise graphitic carbon (e.g., carbon black, graphitic nanotubes, or fullerenes). . . . Conductive microparticles may comprise organic conductors, for example, polypyrrole, polythiophene, polyaniline, and polyacetylene." Col. 4, line 55 to col. 5, line 7 (emphasis added).

To those of ordinary skill in an art, it is generally obvious to alter a known product by substituting a known equivalent for one of its components. See, e.g., Hotchkiss v. Greenwood, 52 U.S. 248 (1850) (substitution of porcelain door knob in known process of making metal or wood door knobs held obvious); In re Mayne, 104 F.3d 1339, 1343, 41 USPQ2d 1451, 1451 (Fed. Cir. 1997) ("Because the applicants merely substituted one element known in the art for a known equivalent, this court affirms [the rejection for obviousness]."); Richardson-Vicks Inc. v. Upjohn Co., 122 F.3d 1476, 1484, 44

USQP2d 1181, 1187 (Fed. Cir. 1997) (The combination of ibuprofen and pseudoephedrine in a single dosage was "clearly suggested by the prior art including CO-TYLENOL®, which combined an analgesic with pseudoephedrine into a single tablet"; "[i]buprofen was a known analgesic that was interchangeable with either aspirin or acetaminophen.").

Here, a skilled artisan would have found it obvious to substitute microparticles made from an organic conductor such as polyaniline for the gold particles used by Kim. The prior art would have suggested such a modification of Kim's device because Sigal teaches that microparticles made from gold and those made from organic conductors were "well known in the art" and were both known to be suitable for applications requiring conductive microparticles.

Appellants argue that the cited references would not have led those skilled in the art to eliminate the gold particles from Kim's system and attach the polyaniline polymers directly to analyte-specific antibodies, because Kim teaches away from that approach. See the Reply Brief, pages 16-18.

It is immaterial whether the references would have led those skilled in the art to modify Kim's system to eliminate the electrically conductive particles altogether. That rationale is not the basis of the rejection. See the Examiner's Answer, page 6 ("[I]t would have been obvious . . . to substitute an organic polyaniline polymer for gold metal.") and page 13 ("Substituting a conductive polymer bead for the gold bead does not negate the necessary placement of the polyaniline strings on the surface.").

Appellants also argue that "[u]sing the polymer beads of Sigal et al. in place of the gold particles of Kim et al. does nothing to solve the conductivity problems

associated with using the gold beads which Kim et al. attempts to resolve. Thus, there is nothing to motivate a person of ordinary skill in the art to use conductive polymer beads to replace the gold particles described by Kim et al." Reply Brief, page 19.

We do not find this argument persuasive. Kim describes the problem that results from using gold beads by themselves in the disclosed device. Kim also discloses that attaching polyaniline "strings" to the gold beads overcomes that problem. Sigal discloses that preparation of conductive microparticles from both gold and organic conductors (e.g., polyaniline) was well known in the art. We therefore agree with the examiner that those of skill in the art would have found it obvious to substitute beads made from an organic conductor (e.g., polyaniline) for the gold beads used by Kim, and attach polyaniline strings to the organic beads, with a reasonable expectation that the organic beads would perform the same function as the gold beads.

Since conductive microparticles made from gold and conductive microparticles made from organic conductors (e.g., polyaniline) were taught in the art to be equivalents, no express suggestion to substitute one for the other is required. See In re Fout, 675 F.2d 297, 301, 213 USPQ 532, 536 (CCPA 1982) ("Because both [prior art references] teach a method for separating caffeine from oil, it would have been prima facie obvious to substitute one method for the other. Express suggestion to substitute one equivalent for another need not be present to render such substitution obvious.")

3. Obviousness based on Kim, Sigal, and Roberts

The examiner also rejected claims 3, 10, 22, 24, and 26 under 35 U.S.C. § 103 as obvious in view of Kim, Sigal, and Roberts.[3] The examiner relied on Kim and Sigal for the disclosures discussed above, but acknowledged that neither reference teaches a multiple array. The examiner cited Roberts for its disclosure of "multiple sets of interdigitated electrode arrays . . . in order to perform simultaneous multiple analyte detection and assay a test sample for a plurality of analytes." Examiner's Answer, pages 7-8. The examiner concluded that "[i]t would have been obvious at the time of the invention to modify the method of Kim et al[.] and Sigal et al[.] with a test device that includes multiple sets of interdigitated electrode arrays . . . as taught by Roberts et al[.], in order to perform simultaneous multiple analyte detection and assay a test sample for a plurality of analytes." Id., page 8.

We agree with the examiner that the device of claim 22 would have been prima facie obvious in view of the cited references. As discussed above, Kim and Sigal show that the device of claim 1 would have been obvious to those of ordinary skill in the art. Claim 22 is directed to the same device, "as a multiple array of devices grouped together separately on the substrate so that multiple analytes can be detected simultaneously from the same sample."

Roberts discloses an immunoassay device in which the signal is measured electrochemically. See column 5, line 55 to column 6, line 30. Roberts also teaches that "[w]ith the test devices and methods of the invention, one may also assay a test sample for a plurality of analytes such as toxic chemicals, or screen for one or more of a

[3] Roberts et al., U.S. Patent 5,958,791, issued Sept. 28, 1999

plurality of analytes. In one embodiment, the test device includes multiple sets of interdigitated electrode arrays. By appropriately controlling the potentials at the electrodes, different marker ions can be measured and referred back to separate analyte concentrations." Col. 25, lines 15-23.

We agree with the examiner that, based this disclosure, "[i]t would have been obvious at the time of the invention to modify the method [and device] of Kim et al[.] and Sigal et al[.] with a test device that includes multiple sets of interdigitated electrode arrays . . . , as taught by Roberts et al[.], in order to perform simultaneous multiple analyte detection and assay a test sample for a plurality of analytes." Examiner's Answer, page 8.

Appellants argue that "a single multiple array as taught by Applicants and illustrated in Figure 3, wherein a plurality of analytes in a mixture can be individually detected at one of the multiple regions 21A to 21D would not be suggested by the cited prior art references." Reply Brief, page 24. See also pages 25-26: "[T]he electrode arrays of Roberts et al., unlike those arrays taught by Applicants, must be maintained at a large enough distance so that no electroactive markers can diffuse over the electrodes in an adjacent measurement portion 106. The design of the device taught by Applicants does not have this problem with cross over signal. . . . [A]ny signal measured across the electrodes of any of the regions 21A to 21D is generated by specific binding of the desired analyte to the region."

This argument does not persuade us of any error in the examiner's rejection. Appellants assert that the device suggested by the prior art differs from the device shown in Figure 3 of the instant application. Even if this assertion is correct, however, it

does not establish any difference between the device suggested by the prior art and the device defined by instant claim 22. Appellants have pointed to no limitation in claim 22 that is not suggested by the prior art, or explained how the language of claim 22 limits it to the embodiment shown in Figure 3. Since Appellants have not distinguished the claimed invention from the prior art, they have not rebutted the examiner's rejection.

Summary

The examiner has shown that claims 1 and 22 would have been obvious to those of ordinary skill in the art. We therefore affirm the rejection of those claims. Claims 2, 7-9, 14-16, 18, 19, and 21 fall with claim 1 and claims 3, 10, 24, and 26 fall with claim 22.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Donald E. Adams)
Administrative Patent Judge)
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Eric Grimes) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
)
Lora M. Green) INTERFERENCES
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